Low Prevalence of Anti-DFS70/LEDGF Antibodies in Patients with Dermatomyositis and Other Systemic Autoimmune Rheumatic Diseases

To the Editor:

We read with interest the article by Mahler, et al. They screened a large number of sequential serum samples and sera from patients with various conditions as well as healthy individuals for anti-dense fine speckled 70 autoantibodies (anti-DFS70ab). Their data confirmed the observations that anti-DFS70ab are significantly more prevalent in healthy individuals than in patients with systemic autoimmune rheumatic diseases (SARD) and that, when they are positive, anti-DFS70ab in SARD are usually accompanied by additional SARD-related antibodies. However, their SARD cohort did not include patients with dermatomyositis (DM). We have confirmed that anti-DFS70ab were less prevalent in our DM cohort than in healthy individuals. We also found some anti-DFS70ab-positive patients with DM who exhibited interesting patterns of change in autoantibody titers in longitudinal sera.

From the serum bank of the Department of Dermatology, Nagoya University Hospital, we used sera from 116 Japanese patients with DM, 108 of which were used in our previous study on anti-TIF1-γ/α (155/140) and anti-Mi-2 autoantibodies. The sera were from 103 patients with adult-onset DM [35 with clinically amyopathic DM, 17 with cancer-associated DM, and 51 with classical DM] and 13 with juvenile DM (6 with clinically amyopathic DM and 7 with classical DM). The definitions of DM, clinically amyopathic DM, cancer-associated DM, and juvenile DM were based on the criteria used in our previous studies. The ages at disease onset were 1 to 80 years (mean 47 yrs). Eighty-one patients were female and 35 were male. This study was approved by the Ethics Committee of Nagoya University Graduate School of Medicine and complied with the Declaration of Helsinki guidelines.

Antinuclear antibody testing was performed by indirect immunofluorescence (IIF) on HEp-2 cell substrates (MBL Co. Ltd.), and anti-DFS70ab levels were measured by ELISA (MBL). DM-specific autoantibodies including anti-Mi-2, anti-TIF1-γ/α, anti-MDA5 (CADM-140), and anti-NXP-2 (MJ) antibodies were measured by the ELISA we developed, which uses in vitro transcription and translation recombinant protein.

The anti-DFS70ab ELISA found 7 positive patients in our DM cohort (6.4%; Figure 1A). Patients were confirmed to have anti-DFS70ab by immunoblotting analysis with bacterially expressed recombinant protein, although 2 of them did not show the characteristic DFS pattern in IIF studies (data not shown). Their clinical features are summarized in Table 1. The findings for the anti-DFS70ab-positive patients did not differ markedly from those for the anti-DFS70ab-negative patients with DM. The frequency of anti-DFS70ab in each DM subset (clinically amyopathic DM, cancer-associated DM, adult classical DM, and juvenile DM) was 9%, 6%, 2%, and 15%, respectively. Five of 7 DM patients with anti-DFS70ab had additional DM-specific autoantibodies. Anti-MDA5 antibodies were found in only 3 anti-DFS70ab-positive patients compared to 28 anti-DFS70ab-negative patients. Anti-TIF1-γ antibodies were present in 1 anti-DFS70ab-positive patient, and anti-NXP-2 antibodies were present in another anti-DFS70ab-positive patient, while they were present in 18 and 5 anti-DFS70ab-negative patients, respectively. Anti-TIF1-α and anti-Mi-2 antibodies were not found. In the other 2 patients with anti-DFS70ab, no DM-specific autoantibodies were detected, although other myositis-specific autoantibodies such as anti-iRNA synthetase antibodies including anti-Jo-1, anti-PL-7, anti-PL-12, anti-EJ, and anti-KS were also investigated. However, serum from one of them revealed many unidentified polypeptides by immunoprecipitation using radiolabeled cell extract (data not shown). These data confirm that, in DM as well, anti-DFS70ab are rarely observed and that, when they are positive, they are usually accompanied by additional DM-specific autoantibodies.

Autoantibodies against MDA5 are a serological marker for DM, especially for clinically amyopathic DM complicated with rapidly progressive interstitial lung disease (ILD), often resulting in poor...
Recently, we showed that anti-MDA5ab disappeared in clinically amyopathic DM complicated with ILD during disease remission. In our DM cohort, we had 3 patients with both anti-DFS70ab and anti-MDA5ab. In addition, we recently encountered another patient with juvenile DM complicated with ILD who had both autoantibodies. Although 1 patient died from rapidly progressive ILD, the other 3 patients (1 juvenile DM patient with rapidly progressive ILD, 1 with chronic ILD, and 1 with amyopathic DM without ILD) have survived. In the deceased patient, the anti-MDA5ab level did not change during the therapy, whereas anti-DFS70ab changed to become negative (Figure 1B). In contrast, in the 3 surviving patients, anti-MDA5ab disappeared upon remission of ILD and/or ADM, whereas anti-DFS70ab levels increased. The hypothesis from the Mahler group that anti-DFS70ab serve as "protective autoantibodies" is very attractive. The patterns of change in anti-DFS70ab titers in the present 4 anti-MDA5-positive patients with DM (1 deceased, 3 surviving) may support the idea of a protective nature of anti-DFS70ab. The higher prevalence of anti-DFS70ab in healthy individuals than in patients with SARD may support this hypothesis. Such a possibility regarding anti-DFS70ab should be explored by future study.

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